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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/560,377 | 06/19/2006 | Catherine J. Pachuk | 051058-034000-US | 3823 |
| 90162 | 7590 | 04/19/2011 | | |
| David S. Resnick | | | EXAMINER | |
| Nixon Peabody LLP | | | PENG, BO | |
| 100 Summer Street | | | ART UNIT | PAPER NUMBER |
| Boston, MA 02110 | | | 1648 | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Art Unit: 1648

Continuation of 11. The request for reconsideration has been considered but does NOT place the application in condition for allowance for following reasons:

(Prior rejection-maintained) The rejection of Claims 63 and 78 under 35 USC 102(b) as being anticipated by Ill (US 5,843,770), is **maintained** for the reason of record and the reason set forth below:

Applicant argues that SEQ ID NO: 1 described by Ill et al. is a single-stranded 587 nucleotide fragment because the Sequence Listing describes that SEQ ID NO:1 is “single” stranded, and “linear”, which is not “double stranded” as required by the claims.

Applicant’s argument is not persuasive. The Sequence Listing requires only the primary sequences of the cited sequences, which are in linear formats. The primary sequence of SEQ ID NO:1 of the prior art, shown in the Sequence Listing, is not the conformation of SEQ ID NO:1. It is noted that the Sequence Listing of the instant application also shows that primary sequences of SEQ ID NOs: 3 and 10 are in “single” stranded and “linear” formats. Thus, Applicant’s argument based on the primary sequence of SEQ ID NO:1 described in the Sequence Listing is not persuasive.

As indicated in the previous Office action (see Para 10), the RNA of SEQ ID NO: 1 of the prior art comprises “at least 19 contiguous base pair nucleotide sequence of the claimed dsRNA SEQ ID NO: 10”. One of ordinary skill in the art knows that RNA inherently forms “a double-stranded conformation”.

According to MPEP 2112.0, “Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product”.

Applicant has not presented any factual evidence that the nucleic acid sequence of SEQ ID NO:1 of the prior art is not capable of forming a double-stranded conformation. For the reasons set forth above, the rejection is maintained.

(Prior rejection-maintained) The rejection of Claims 63 and 78 under 35 USC 102(b) as being anticipated by Sallberg (US20020155124, published on October 24, 2002; Now US Pat. 6,680,059), is **maintained** for the reason of record.

In response to Applicant’s argument:

Applicant presents the same argument as Sallberg et al. does not teach or suggest that such DNA/RNA hybrids are administered or formed, particularly in vivo. One of skill in

the art One of skill in the art would understand that double-stranded DNA does not typically generate a DNA/RNA hybrid in vivo. Similarly, while Applicants agree that under the proper conditions, double-stranded DNA can be transcribed in vivo to produce a single-stranded mRNA,

This argument is not persuasive. Sallberg teaches methods of enhancing the immune response of an animal, including humans, using HBV nucleic acid-based antigen, wherein said nucleic acid-based antigens include a nucleotide sequence of HBV SEQ ID No: 14, see e.g. [0017] and [0041]. Sallberg also teaches that a nucleic acid-based antigen can comprise at least 9-25, 25-50, 50-100, 100-200, 200-500, 500-1000, 1000-2000, or 2000-4000 consecutive nucleotides of any one of SEQ ID NO: 14 or **an RNA** that corresponds to these sequences. Given that an RNA of SEQ ID NO:14 has same sequence as the instant SEQ ID NO:3, one of ordinary skill in the art would understand that the RNA of prior art would inherently form a double-stranded conformation as the RNA of the instant claims.

16. **(Prior rejection-maintained)** The rejection of Claims 63-67, 78 and 79 under 35 USC 103(a) as being unpatentable over Ill (US 5,843,770), Sallberg (US2002/0155124), and McCaffrey (Nature Biotechnology, 21(6):639-644; published online May 12, 2003), **is maintained** for the reason of record.

In response to Applicant's arguments:

Applicant presents the same arguments as above that the Ill et al. and Sallberg et al. references do not teach double stranded RNA corresponding to any sequence, let alone double stranded RNA comprising at least 19 contiguous base pair nucleotide sequence in a double-stranded conformation from within a sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 10, wherein U is substituted for T. Moreover, McCaffrey does not teach SEQ ID NOS: 3 and 10. The combined teaching fails to teach all elements of the claims.

Applicant's arguments against the Ill et al. and Sallberg et al. references have been found not persuasive above. Applicant's argument against McCaffrey alone is not persuasive, either, because the cited Ill and Sallberg references teach dsRNA effector molecules comprising at least 19 contiguous base pair nucleotide sequence in a double-stranded conformation from with SEQ ID NO: 3 or SEQ ID NO: 10. Thus, the combined teaching has taught all elements of the claims. Also see Para 20 the Final Office action. The rejection is maintained.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you

have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Primary Examiner, Art Unit 1648

| | | |
|--|--------------------------------------|--------------------------------------|
| <i>Advisory Action Before the Filing of an Appeal Brief</i> | Application No. 10/560,377 | Applicant(s) PACHUK ET AL. |
| | Examiner BO PENG | Art Unit 1648 |

-The MAILING DATE of this communication appears on the cover sheet with the correspondence address -

THE REPLY FILED 17 November 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) The period for reply expires _____ months from the mailing date of the final rejection.
 - b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. The Notice of Appeal was filed on 16 February 2011. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
- (a) They raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) They raise the issue of new matter (see NOTE below);
 - (c) They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) They present additional claims without canceling a corresponding number of finally rejected claims.
- NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. Applicant's reply has overcome the following rejection(s): _____.
6. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. For purposes of appeal, the proposed amendment(s): a) will not be entered, or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 63-67, 78 and 79.

Claim(s) withdrawn from consideration: 98-101.

AFFIDAVIT OR OTHER EVIDENCE

8. The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. The request for reconsideration has been considered but does NOT place the application in condition for allowance because: The request for reconsideration has been considered but does NOT place the application in condition for allowance for following reasons: see attached Continuation.
12. Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. Other: _____.

/BO PENG/
Primary Examiner, Art Unit 1648